

Amendments to the claims:

Please amend claims 1, 16, 23, 24, 25, 27, 28, 30, 31, and 33. Please cancel claims 26 and 29. This listing of claims replaces all prior versions and listings of claims in the application:

Listing of claims:

1. (Currently Amended) A method of detecting ras-activated neoplastic cells in a biological sample, comprising contacting the sample with a reovirus under conditions which allow the reovirus to replicate in ras-activated cells, [[and]] determining the ability of the reovirus to replicate in the sample, and identifying the sample as comprising ras-activated neoplastic cells if the reovirus can replicate in the sample ~~wherein the ability of the reovirus to replicate indicates the presence of ras-activated neoplastic cells in the sample.~~
2. (Original) The method of claim 1 wherein the biological sample is from a mammal.
3. (Original) The method of claim 2 wherein the mammal is human.
4. (Original) The method of claim 1 wherein the reovirus is a mammalian reovirus.
5. (Original) The method of claim 4 wherein the mammalian reovirus is a serotype 3 reovirus.
6. (Original) The method of claim 5 wherein the serotype 3 reovirus is a Dearing strain reovirus.

7. (Withdrawn) The method of claim 1 wherein the reovirus is an avian reovirus.
8. (Original) The method of claim 1 wherein the biological sample is from an animal bearing a neoplasm selected from the group consisting of lung cancer, prostate cancer, colorectal cancer, thyroid cancer, renal cancer, adrenal cancer, liver cancer, pancreatic cancer, breast cancer, hematopoietic cancer and central and peripheral nervous system cancer.
9. (Original) A method of diagnosing a ras-activated neoplasm in an animal, comprising:
  - (a) providing a biological sample from the animal, wherein the sample comprises cells;
  - (b) contacting the sample with a reovirus under conditions which allow the reovirus to replicate in ras-activated cells;
  - (c) determining the ability of the reovirus to replicate in the sample; and
  - (d) identifying the animal as having a ras-activated neoplasm if the reovirus can replicate in the sample.
10. (Original) The method of claim 9 wherein the animal is human.
11. (Original) The method of claim 9 wherein the reovirus is a mammalian reovirus.
12. (Original) The method of claim 11 wherein the mammalian reovirus is a serotype 3 reovirus.
13. (Original) The method of claim 12 wherein the serotype 3 reovirus is a Dearing strain reovirus.

14. (Withdrawn) The method of claim 9 wherein the virus is an avian reovirus.
15. (Original) The method of claim 9 wherein the biological sample is from a neoplasm selected from the group consisting of lung cancer, prostate cancer, colorectal cancer, thyroid cancer, renal cancer, adrenal cancer, liver cancer, pancreatic cancer, breast cancer, hematopoietic cancer and central and peripheral nervous system cancer.
16. (Withdrawn, currently amended) A method of treating or ameliorating a ras-activated neoplasm in an animal, comprising:
  - (a) identifying a ras-activated neoplasm in the animal by providing a group of cells from the animal, contacting the cells with a reovirus under conditions which allow the reovirus to replicate in ras-activated cells, determining the ability of the reovirus to replicate in the cells, and identifying the cells as comprising ras-activated neoplastic cells if the reovirus can replicate in the cells; and
  - (b) administering to the animal an effective amount of a therapeutic agent that is selective for ras-activated neoplasms.
17. (Withdrawn) The method of claim 16 wherein the therapeutic agent is an oncolytic virus selected from the group consisting of reoviruses, adenoviruses mutated in the VA1 region, vaccinia viruses mutated in the K3L and/or E3L region, parapoxvirus orf viruses mutated in the OV20.0L gene, influenza viruses mutated in the NS-1 gene, and herpes viruses mutated in the  $\gamma$ 134.5 gene.
18. (Withdrawn) The method of claim 16 wherein the animal is a mammal.
19. (Withdrawn) The method of claim 18 wherein the mammal is human.

20. (Withdrawn) The method of claim 16 wherein the reovirus is a mammalian reovirus or avian reovirus.
21. (Withdrawn) The method of claim 16 wherein the reovirus is a Dearing strain reovirus.
22. (Withdrawn) The method of claim 16 wherein the biological sample is from a neoplasm selected from the group consisting of lung cancer, prostate cancer, colorectal cancer, thyroid cancer, renal cancer, adrenal cancer, liver cancer, pancreatic cancer, breast cancer, hematopoietic cancer and central and peripheral nervous system cancer.
23. (Currently amended) A method of diagnosing the presence of a neoplasm in a mammal, comprising contacting a sample of cells from said mammal with an oncolytic virus under conditions which allow the oncolytic virus to replicate in neoplastic cells, wherein the ability of said virus to duplicate in said sample indicates the presence of a neoplasm in said mammal, provided the oncolytic virus is not an adenovirus.
24. (Currently amended) The method of claim 23 wherein the virus is selected from the group consisting of reoviruses, ~~adenoviruses mutated in the VA1 region~~, vaccinia viruses mutated in the K3L and/or E3L region, parapoxvirus orf viruses mutated in the OV20.0L gene, influenza viruses mutated in the NS-1 gene, herpes viruses mutated in the  $\gamma_1$ 34.5 gene, and vesicular stomatitis virus, ~~ONYX-015 virus, and Delta24 virus~~.
25. (Currently Amended) A method of detecting neoplastic cells in a biological sample, the neoplastic cells having a particular phenotype selected from ras pathway activation, interferon-resistance, p53-deficiency and Rb-deficiency in a biological sample, comprising contacting the sample with an oncolytic virus that selectively replicates in neoplastic cells having the particular phenotype under conditions which allow the oncolytic virus to selectively replicate in said neoplastic cells, [[and]] determining the

ability of the virus to replicate in the sample, and identifying the sample as comprising neoplastic cells having the particular phenotype if the oncolytic virus can replicate in the sample wherein the ability of the virus to replicate indicates the presence of neoplastic cells having the particular phenotype in the sample, provided the oncolytic virus is not an adenovirus.

26. (Canceled)
27. (Withdrawn, currently amended) The method of claim 25 wherein the virus is selected from the group consisting of:
- (a) ~~vesicular stomatitis virus,[[;]]~~
  - (b) ~~ONYX 015 virus;~~
  - (c) ~~Delta24 virus; and~~
  - (d) ~~a virus selected from the group consisting of adenoviruses mutated in the VA1 region, vaccinia viruses mutated in the K3L and/or E3L region, parapoxvirus orf viruses mutated in the OV20.0L gene, influenza viruses mutated in the NS-1 gene, and herpes viruses mutated in the  $\gamma$ 134.5 gene.~~
28. (Currently Amended) A method of diagnosing a neoplasm having a particular phenotype in an animal, comprising:
- (a) providing a biological sample from the animal, wherein the sample comprises cells;
  - (b) contacting the sample with an oncolytic virus that selectively replicates in neoplastic cells having the particular phenotype under conditions which allow the oncolytic virus to selectively replicate in said neoplastic cells, provided the oncolytic virus is not an adenovirus;
  - (c) determining the ability of the virus to replicate in the sample; and

- (d) identifying the animal as having a neoplasm having the particular phenotype if the virus can replicate in the sample,  
wherein the particular phenotype is selected from the group consisting of interferon-resistance, p53-deficiency, Rb-deficiency, and PKR-deficiency.

29. (Canceled)

30. (Withdrawn, currently amended) The method of claim 28 wherein the virus is selected from the group consisting of:

- (i) ~~vesicular stomatitis virus,[[;]]~~
- (ii) ~~ONYX 015 virus;~~
- (iii) ~~Delta24 virus; and~~
- (iv) ~~a virus selected from the group consisting of adenoviruses mutated in the VA1 region, vaccinia viruses mutated in the K3L and/or E3L region, parapoxvirus orf viruses mutated in the OV20.0L gene, influenza viruses mutated in the NS-1 gene, and herpes viruses mutated in the  $\gamma_1$ 34.5 gene.~~

31. (Withdrawn, currently amended) A method of treating or ameliorating a neoplasm having a particular phenotype in an animal, comprising:

- (a) identifying a neoplasm having a particular phenotype in the animal by providing a group of cells from the animal, contacting the cells with an oncolytic virus that selectively replicates in neoplastic cells having the particular phenotype, determining the ability of the oncolytic virus to replicate in the cells, and identifying the cells as comprising a neoplasm having the particular phenotype if the virus can replicate in the cells;
- (b) administering to the animal an effective amount of a therapeutic agent that is selective for neoplastic cells having the particular phenotype.

32. (Withdrawn) The method of claim 31 wherein the particular phenotype is selected from the group consisting of interferon-resistance, p53-deficiency, Rb-deficiency, and PKR-deficiency.
33. (Withdrawn, currently amended) The method of claim 31 wherein the virus is selected from the group consisting of:
- (i) ~~vesicular stomatitis virus~~<sub>1</sub>[[;]]
  - (ii) ~~ONYX-015 virus~~;
  - (iii) ~~Delta24 virus~~; and
  - (iv) ~~a virus selected from the group consisting of adenoviruses mutated in the VA1 region~~, vaccinia viruses mutated in the K3L and/or E3L region, parapoxvirus orf viruses mutated in the OV20.0L gene, influenza viruses mutated in the NS-1 gene, and herpes viruses mutated in the  $\gamma$ 134.5 gene.